Thermophysical studies on molecular interactions of neurotransmitters in different aqueous media

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Submitted by

Miss. Nita Tukaram Rasal

(M.Sc. SET, GATE)

Under The Supervision of

Dr. Atmaram D. Arsule

(M.Sc., NET, SET, GATE , Ph.D.)

Assistant Professor

Dr. S. D. Deosarkar

(M.Sc. (Gold medal), SET, Ph.D.)

Professor and Director

School of chemical science, S. R. T. M. University, Nanded

School of Chemical Sciences Swami Ramanand Teerth Marathwada University, Vishnupuri, Nanded-431606

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Ph. D. Synopsis / Work plan

Abstract of Proposed work plan/problem**,** Entitled ***"Thermophysical studies on molecular interactions of neurotransmitters in different aqueous media"***

1. Introduction

Neurotransmitters are the endogenous chemicals that allow neurons to communicate with each other throughout the body. They enable the brain to provide a variety of functions, through the process of chemical synaptic transmission. Their job is to carry chemical signals from one neuron to the next target cell. They either stimulate or inhibit electrical impulses in target cells. They are categorized into three major groups i.e. amino acids, peptides and monoamines. The previous studies indicate that the most widely distributed neurotransmitters belong to a class of compounds referred to as amino acids. These small molecules are present at high concentrations in all cells probably because of their key role in protein synthesis and metabolism.

There are some major neurotransmitters: Glutamate, γ-aminobutyric acid, Dopamine, Adrenaline, Serotonin, Oxytocin and Acetylcholine etc. The γ-Aminobutyric acid (GABA) is the main inhibitory neurotransmitter, present in all areas of the central nervous system (CNS). In fact, as many as 10–40% of nerve terminals in the cerebral cortex, hippocampus and substantia nigra may use GABA as a neurotransmitter. GABA is administered as a potential drug for psychiatric and neurological disorders including anxiety, depression, insomnia and epilepsy. It is used for stabilizing blood pressure, relieving pain and treating attention deficithyperactivity disorder (ADHD).

Glycine is the second major inhibitory neurotransmitter in the CNS. It play important role as a neurotransmitter has been most conclusively established in inhibitory interneurons in the spinal cord. Glycine and its salts are the major inhibitory neurotransmitters in the brainstem and spinal cord, where they participate in a variety of motor and sensory functions. It promotes the actions of glutamate, a major excitatory neurotransmitter in the brain. Thus, glycine serves both inhibitory and excitatory functions within the CNS.

Glutamic acid, is a crystalline dibasic nonessential amino acid, inhibiting neural excitation in the central nervous system. Sodium glutamate is used in treating encephalopathies associated with hepatic diseases and to enhance the flavor of foods. Interaction of drugs

with bio-macromolecules in the receptor sites is an important phenomenon in physiological media such as blood, membranes and intra/extra-cellular fluids.

Water is the matrix of life and the host of most biological processes, particularly in its cooperative interactions with proteins. The drug-water molecular interactions and their temperature dependence play an important role in understanding drug action. Therefore, it is imperative to study drug interactions in aqueous media thermodynamically by monitoring different volumetric and acoustic properties which are vital in understanding molecular interactions (hydrophilic, hydrophobic and ionic interactions) as they provide perceptible parameters for the elaboration of solute-solvent and solute-solute interactions in the solution phase.

The most important and interesting field in medicine and pharmaceutical and industrial chemistry which has advance over a two decade work done by groups of neurochemists for the discovery of chemical messengers. The simplest neurotransmitters are Glutamate, γ-aminobutyric acid, Noradrenaline, Dopamine, Adrenaline, Serotonin, Oxytocin and Acetylcholine etc. Deficiency of dopamine is found to result in Parkinson's disease and its over-firing causes some forms of paranoid schizophrenia and may be treated with L-dihydroxyphenylalanine (L-DOPA).

Thermophysical properties such as density, ultrasonic velocity, refractive index of chemical messengers in different aqueous media at different temperatures are very rare or very lesser amount of work done by the research groups. There has been no attempt to investigate their thermophysical properties of chemical messengers. Our Scientific approach to study thermodynamic properties of chemical messengers/neurotransmitters in different aqueous media to furnish the significant information to understanding the molecular interactions.

2. Review of Literature and Development in the Subject (Previous work done in the relevant area):

- E.C.Hulme et al. have studied the hydration of the neurotransmitter acetylcholine in aqueous solution.
- J.M.Moses et al. have studied on molecular interactions of some neurotransmitters in water using volumetric and compressibility measurements at T=(278.15,288.15 and 298.15)K.

- M. M. Rodrigo et al. have studied the structure and diffusion behaviour of the neurotransmitter gama-aminobutyric acid (GABA) in neutral aqueous solution.
- A. J. Shah, F. Crespi and C. Heidbreder have studied amino acid neurotransmitters: separation approaches and diagnostic value.
- N.G. Bowery and T.G.Smart have studied GABA and glycine as neurotransmitters: a brief history.
- M.V. Fedotova, S.E. Kruchinin and G.N. Chuev have studied hydration features of the neurotransmitter acetylcholine.
- A. Bagheri Gh have studied thermodynamic studies on complexation of dopamine with gadolinium water-ethanol system.
- A. Bagheri and D.M.Boghael have studied thermodynamic studies on the complexation of cobalt with dopamine in a cosolvent system.
- M. Dyck et al. have studied interaction of the neurotransmitter, neuropeptide Ywith phospholipid membranes:infrared spectroscopic characterization at the air/water interface.
- P. I. Nagy et al. have studied theoretical conformational analysis for neurotransmitters in the gas phase and in aqueous rine. Norepinephrine.
- F. Shahidi has studied partial molar volumes of phenylalkylamines and their physiologically active derivatives in water.

3. Objectives of Research / Proposed hypothesis

- Objective of the proposed work is to understand in depth the molecular interactions among neurotransmitters and drug, salt, sugar in different aqueous media through the study of volumetric, optical and thermo-acoustic properties.
- To calculate apparent molar, partial molar volume and transfer volume of neurotransmitters in studied systems and evaluation of the same in terms of structural fittings and molecular interaction in aqueous solution.
- To compute the thermo-acoustic properties from density and ultrasonic velocity data and interpretation in terms of molecular interaction in solution.
- To analyze the refractive index data for the neurotransmitter in aqueous system.
- To study the thermophysical parameters for neurotransmitters and molecular interactions with aqueous media on volumetric, optical and thermo-acoustical properties.

4. Methodology to be adopted

Quantitative measurements of various thermo-acoustical/physicochemical properties such as density, sound velocity, refractive index etc. of neurotransmitters in aqueous media will be carried out. Measurements of densities will be carried out by using single capillary pycnometer on one pan electronic balance. Sound velocity (ultrasonic velocity) of neurotransmitters in different aqueous media will be measured using ultrasonic interferometer of fixed frequency (Model-F05, Mittal, 2 ± 0.0001 MHz). Refractive index measurements of neurotransmitters will be done using thermostatically Abbes refractometer. Refractive index measurements were performed on thermostatically controlled Cyber LAB-Cyber Abbe Refractometer (Amkette Analytics, ±0.0002, 1.3000 to 1.7000). Refractometer was calibrated using standard specimen (n=1.5167).

Various properties will be measured for the specified conditions like temperature, pressure, neurotransmitter concentration and various aqueous media for the respective systems. The experimental properties like density, sound velocity, refractive index etc. will be used to calculate various derived volumetric, acoustical and refractometric etc. properties for the studied neurotransmitters.

5. Importance of study/society application:

Interaction of neurotransmitters with drugs, sugar and salt in different mediaplay an important role for their activities like drug actions i.e. drug reaching the blood stream, its extent of distribution, its binding to the receptors and finally producing physiological action, all depend on various physicochemical properties chiefly detected by various interactions. The variety and complexity of (solute + solvent) interactions in case of aqueous solutions of amino acid neurotransmitters have resulted in numerous investigations of the solvation behaviour The drug-water molecular interactions and their temperature dependence play an important role in understanding drug action. Therefore, it is imperative to study drug interactions in aqueous media thermodynamically by monitoring different volumetric and acoustic properties which are vital in understanding molecular interactions (hydrophilic, hydrophobic and ionic interactions) as they provide perceptible parameters for the elaboration of solute-solvent and solute-solute interactions in the solution phase.

International status

Following researchers are working on the study of molecular interactions in different neurotransmitter solutions in different media at the international level:

1) Changwei Zhao, Peisheng Ma, Jiding Li, Department of Chemical Engineering, Tsinghua University, Beijing, PR China. This team has worked on Partial molar Fereidoon Shahid, Department of Biochemistry, Memorial University of Newfoundland, St. John's, Nfld., Canada. This research group worked on thermodynamic properties of phenalkylamines and their physiologically active derivatives with different aqueous medium has been collected.
2) D. P. Kharakor, Institute of Bio/Physics, Academy of Sciences of the USSR, Puschino, Moscow Region, USSR. This team worked on thermophysical properties of amino acid and protein.
3) Evgeniy V. Ivanov etal Laboratory of Thermodynamics of Solutions of Non-electrolyte and Biologically Active Substances, G.A. Krestov Institute of Solution Chemistry, Russian Academy of Sciences, 1 Akademicheskaya Str., 153045 Ivanovo, Russian Federation. This research group is worked on physiochemical properties of protein, glycolurils, electrolyte, non- electrolyte, vitamin and peptides in different aqueous media.
4) Markus Hofmann, Exhibition Rd, South Kensington, London SW7 2BX, United Kingdom, Imperial College London. This research group is worked on density, viscosity, refractive index and speed of sound of different biomolecule in different aqueous media.
5) Jan Antosiewicz, Faculty of chemistry, Jagiellonion University, Karasia and Department of Biophysics, University Warsaw, Poland. This group has studied on sound velocity of carbohydrate/sugar in aqueous solution.
6) Changwei Zhao, Peisheng Ma, Jinding Li, Department of Chemical Engineering, Tsinghua University, Beijing, PR China. This team has worked on Partial molar volumes and viscosity B-coefficients of arginine in aqueous glucose, sucrose and L-ascorbic acid solution

- **National status**

Following researchers are working on the study of molecular interactions in different neurotransmitter solutions in different media at the national level:

1) R. Palani, G. Srinivasan and B. Geeta Lakshmi, Department of physics, Annamalia University, Tamil Nadu, India.

2) Tarlok S. Banipal, Jasbir Kaur, Parampaul K. Banipal, Ashwani K. Sood, and Kultar Singh, Department of Chemistry, Guru Nanak Dev University, Amritsar-143005, Punjab, India.
3) Santosh D. Deosarkar, School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Nanded- 431606 (*MS*). This research group worked on biologically important drugs, amino acids, carbohydrate and vitamins.
4) Anwar Ali, Soghra Hyder, Saba Sabir, Dinesh Chand, Anil Kumar Nain, Department of Chemistry, Jamia Millia Islamia (Central University), New Delhi 110 025, India.
5) Riyazuddeen and Sadaf Afrin, Department of Chemistry, Aligarh Muslim University, Aligarh 202002, U.P., India.
6) Amalendu Pal, Nalin Chauhan, Department of Chemistry, Kurukshetra University, Kurukshetra-136119, India.

- **Significance of the study**

To understand the nature of interaction of neurotransmitter with aqueous solution of sugar, salts and drugs by means of the systematic measurements of Densities (p), speeds of sound (u), viscosities (η) and parameters such as the partial molar volumes(ϕv^o), transfer partial molar volumes ($\Delta tr\phi v^o$), isentropic compressibility (ks), partial molar isentropic compressibility (ϕk^o), transfer partial molar isentropic compressibility($\Delta tr\phi k^o$) and viscosity Coefficient. On the basis of these Thermo-physical parameters we will obtain the data about molecular interaction like, neurotransmitter-sugars, neurotransmitter-salts and neurotransmitter-drugs molecular. Investigation on the thermodynamic properties to provide significance information that, ultimately lead to better understanding of behavior of neurotransmitter with organic molecule like sugar, salts and drugs.

6. Proposed work Plan/ Formulation and Structure of Study:

Year-wise Plan of work and targets to be achieved

In present research proposal, the thermodynamic properties (density, ultrasonic velocity and refractive index) of neurotransmitters will be studied in aqueous medium containing different co-solutes like sugar, salts and drugs. The aqueous systems of neurotransmitters in two sugars, two salts and two drugs will be studied. The year-wise plan of the work is as below:

- **First year:** The thermodynamic properties of neurotransmitters in aqueous solutions of sugar will be carried out. The study will be carried out for different concentrations of the neurotransmitters, different temperatures and different concentrations of the co-solute, sugar.
- **Second year:** The thermodynamic properties of neurotransmitter in aqueous solutions of drugs will be carried out. The investigation of molecular interactions of neurotransmitters in aqueous solutions of two drugs will be carried out at different temperatures and different concentrations of the co-solute drugs.
- **Third year:** Calculations and interpretation of different thermodynamic properties of studied solutions. Communication of the results to conferences, National and International journals.

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Signature	Signature	Signature
Research Scholar	**Research Co-Guide**	**Research Guide**
(Miss. Nita T. Rasal)	(Dr. S.D Deosarkar)	(Dr. Atmaram D. Arsule)